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Synthetic intestinal mucosal barrier using a hydrogel slab integrated microfluidic chip

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The mucosal barrier lining along the intestinal tract plays a key role in metabolic and immunological homeostasis. Repeated disruption of the mucosal barrier integrity has been suggested to be a precursor event that derives inflammatory bowel diseases and colorectal cancer. Multiple in vitro platform technologies have been developed to understand the mucosal barrier function including trans-wells and microfabricated devices, but a static and vertical axis culture settings limits to simulate and observe dynamic complexity of the gut microenvironment. Here, we introduce a biomaterials engineering approach to create a synthetic mucosal barrier in a transverse manner for direct observation of cellular processes. A type I collagen hybridized polyacrylamide hydrogel supporting small molecular transport and epithelial cell adhesion was used as a framework and subsequently anchored covalently to a glass slide via silanization chemistry. Villous microstructures ~250µm in height were manufactured by casting the hydrogel precursor solution in a pre-designed, removable polydimethylsiloxane micropattern mold and polymerizing using UV light. After sealing the device with another glass slide, we increased the cellular and extracellular complexity of this microfluidic chip by sequentially introducing (i) HT-29 colon epithelial cells, (ii) mucin extracts from a pig intestine, (iii) bacteria, and (iv) human peripheral blood-derived mononuclear cells and co-cultured them in a single device. This modular in vitro microphysiological intestinal tissue model may serve as a translational platform to discover the biophysical etiology for disruption of the mucosal barrier and associated inflammatory diseases.

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